

PATENT COOPERATION TREATY

PCT

NOTIFICATION CONCERNING
SUBMISSION OR TRANSMITTAL
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

From the INTERNATIONAL BUREAU

To: LAM/KYL/CAGGARRETT Arthur, S.
Finnegan, Henderson, Farabow,
Garrett, & Dunner, L
1300 I Street, N.W.
Washington, D.C. 20005-3315
United States of America

Date of mailing (day/month/year) 02 July 2004 (02.07.2004)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 7680.023-304	
International application No. PCT/US2004/013677	International filing date (day/month/year) 30 April 2004 (30.04.2004)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 30 April 2003 (30.04.2003)
Applicant GENZYME CORPORATION et al	

- By means of this Form, which replaces any previously issued notification concerning submission or transmittal of priority documents, the applicant is hereby notified of the date of receipt by the International Bureau of the priority document(s) relating to all earlier application(s) whose priority is claimed. Unless otherwise indicated by the letters "NR", in the right-hand column or by an asterisk appearing next to a date of receipt, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- (If applicable) The letters "NR" appearing in the right-hand column denote a **priority document which, on the date of mailing of this Form, had not yet been received by the International Bureau** under Rule 17.1(a) or (b). Where, under Rule 17.1(a), the priority document must be submitted by the applicant to the receiving Office or the International Bureau, but the applicant fails to submit the priority document within the applicable time limit under that Rule, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- (If applicable) An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a **priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b)** (the priority document was received after the time limit prescribed in Rule 17.1(a) or the request to prepare and transmit the priority document was submitted to the receiving Office after the applicable time limit under Rule 17.1(b)). Even though the priority document was not furnished in compliance with Rule 17.1(a) or (b), the International Bureau will nevertheless transmit a copy of the document to the designated Offices, for their consideration. In case such a copy is not accepted by the designated Office as priority document, Rule 17.1(c) provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
30 April 2003 (30.04.2003)	60/466,417	US	24 June 2004 (24.06.2004)

RECEIVED

JUL 15 2004

Finnegan, Henderson, Farabow,
Garrett & Dunner, L.L.P.

Authorized officer

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PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

FIRST NOTICE INFORMING THE APPLICANT OF
THE COMMUNICATION OF THE INTERNATIONAL
APPLICATION (TO DESIGNATED OFFICES WHICH
DO NOT APPLY THE 30 MONTH TIME LIMIT
UNDER ARTICLE 22(1))

(PCT Rule 47.1(c))

To: LAM/KAL/CAG

GARRETT Arthur, S.
Finnegan, Henderson, Farabow, Garrett, & Dunner, L
1300 I Street, N.W.
Washington, D.C. 20005-3315
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 02 December 2004 (02.12.2004)		
Applicant's or agent's file reference 7680.023-304		IMPORTANT NOTICE
International application No. PCT/US2004/013677	International filing date (day/month/year) 30 April 2004 (30.04.2004)	Priority date (day/month/year) 30 April 2003 (30.04.2003)
Applicant GENZYME CORPORATION et al		

- ATTENTION:** For any designated Office(s), for which the time limit under Article 22(1), as in force from 1 April 2002 (30 months from the priority date), **does apply**, please see Form PCT/IB/308(Second and Supplementary Notice) (to be issued promptly after the expiration of 28 months from the priority date).
- Notice is hereby given that the following designated Office(s), for which the time limit under Article 22(1), as in force from 1 April 2002, **does not apply**, has/have requested that the communication of the international application, as provided for in Article 20, be effected under Rule 93bis.1. The International Bureau has effected that communication on the date indicated below:
18 November 2004 (18.11.2004)

CH

In accordance with Rule 47.1(c-bis)(i), those Offices will accept the present notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

- The following designated Offices, for which the time limit under Article 22(1), as in force from 1 April 2002, **does not apply**, have not requested, as at the time of mailing of the present notice, that the communication of the international application be effected under Rule 93bis.1:

FI, LU, SE, TZ, UG, ZM

In accordance with Rule 47.1(c-bis)(ii), those Offices accept the present notice as conclusive evidence that the Contracting State for which that Office acts as a designated Office does not require the furnishing, under Article 22, by the applicant of a copy of the international application.

4. TIME LIMITS for entry into the national phase

For the designated Office(s) listed above, and unless a demand for international preliminary examination has been filed before the expiration of **19 months** from the priority date (see Article 39(1)), the applicable time limit for entering the national phase will, **subject to what is said in the following paragraph**, be **20 MONTHS** from the priority date.

In practice, time limits other than the 20-month time limit will continue to apply, for various periods of time, in respect of certain of the designated Offices listed above. For regular updates on the applicable time limits (20 or 21 months, or other time limit), Office by Office, refer to the *PCT Gazette*, the *PCT Newsletter* and the *PCT Applicant's Guide*, Volume II, National Chapters, all available from WIPO's Internet site, at <http://www.wipo.int/pct/en/index.html>.

It is the applicant's sole responsibility to monitor all these time limits.

RECEIVED

DEC 14 2004

Finnegan, Henderson, Farabow,
Garrett & Dunner, L.L.P.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Agnes Wittmann-Regis
Facsimile No.+41 22 740 14 35	Facsimile No.+41 22 338 89 70

From the INTERNATIONAL BUREAU

PCTSECOND AND SUPPLEMENTARY NOTICE
INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION (TO DESIGNATED OFFICES
WHICH APPLY THE 30 MONTH TIME
LIMIT UNDER ARTICLE 22(1))

(PCT Rule 47.1(c))

To:

LAM/KXL/MCS

GARRETT Arthur, S.
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1300 I Street, N.W.
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ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)

01 September 2005 (01.09.2005)

Applicant's or agent's file reference

7680.023-304

IMPORTANT NOTICE

International application No.

PCT/US2004/013677

International filing date (day/month/year)

30 April 2004 (30.04.2004)

Priority date (day/month/year)

30 April 2003 (30.04.2003)

Applicant

GENZYME CORPORATION et al

- ATTENTION:** For any designated Office(s), for which the time limit under Article 22(1), as in force from 1 April 2002 (30 months from the priority date), **does not apply**, please see Form PCT/IB/308(First Notice) issued previously.
- Notice is hereby given that the following designated Office(s), for which the time limit under Article 22(1), as in force from 1 April 2002, **does apply**, has/have requested that the communication of the international application, as provided for in Article 20, be effected under Rule 93bis.1. The International Bureau has effected that communication on the date indicated below:
18 November 2004 (18.11.2004)

AU, AZ, BY, CN, CO, DZ, EP, HU, KG, KP, KR, MD, MK, MZ, NA, RU, SY, TM, US

In accordance with Rule 47.1(c-bis)(i), those Offices will accept the present notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

- The following designated Offices, for which the time limit under Article 22(1), as in force from 1 April 2002, **does apply**, have not requested, as at the time of mailing of the present notice, that the communication of the international application be effected under Rule 93bis.1:

AE, AG, AL, AM, AP, AT, BA, BB, BG, BR, BW, BZ, CA, CR, CU, CZ, DE, DK, DM, EA, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KZ, LC, LK, LR, LS, LT, LV, MA, MG, MN, MW, MX, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, SC, SD, SG, SK, SL, TJ, TN, TR, TT, UA, UZ, VC, VN, YU, ZA, ZW

In accordance with Rule 47.1(c-bis)(ii), those Offices accept the present notice as conclusive evidence that the Contracting State for which that Office acts as a designated Office does not require the furnishing, under Article 22, by the applicant of a copy of the international application.

4. TIME LIMITS for entry into the national phase

For the designated or elected Office(s) listed above, the applicable time limit for entering the national phase will, **subject to what is said in the following paragraph**, be **30 MONTHS** from the priority date.

In practice, **time limits other than the 30-month time limit** will continue to apply, for various periods of time, in respect of certain of the designated or elected Office(s) listed above. For **regular updates on the applicable time limits** (30 or 31 months, or other time limit), Office by Office, refer to the *PCT Gazette*, the *PCT Newsletter* and the *PCT Applicant's Guide*, Volume II, National Chapters, all available from WIPO's Internet site, at <http://www.wipo.int/pct/en/index.html>.

It is the applicant's **sole responsibility** to monitor all these time limits.

The International Bureau of WIPO
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Agnes Wittmann-Regis

✓ JDS
9/9/05

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Facsimile No.+41 22 338 89 70

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/013677

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A61K39/395 A61P13/12
 //(A61K39/395,31:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>ZOJA CARLA ET AL: "How to fully protect the kidney in a severe model of progressive nephropathy: a multidrug approach." JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY : JASN. DEC 2002, vol. 13, no. 12, December 2002 (2002-12), pages 2898-2908, XP002289844 ISSN: 1046-6673 abstract</p> <p style="text-align: center;">----- -/---</p>	1-38

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *G* document member of the same patent family

Date of the actual completion of the international search

28 July 2004

Date of mailing of the international search report

29/09/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
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Authorized officer

Lechner, O

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/013677

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	CHEN SHELDON ET AL: "Reversibility of established diabetic glomerulopathy by anti-TGF-beta antibodies in db/db mice." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 300, no. 1, 3 January 2003 (2003-01-03), pages 16-22, XP002289845 ISSN: 0006-291X abstract	1-38
Y	GAEDEKE JENS ET AL: "Angiotensin II and progressive renal insufficiency." CURRENT HYPERTENSION REPORTS. OCT 2002, vol. 4, no. 5, October 2002 (2002-10), pages 403-407, XP009034388 ISSN: 1522-6417 abstract page 404, right-hand column, paragraph 1	1-38
Y	WO 01/66140 A (GENZYME CORP ; ROMAN RICHARD J (US); LEDBETTER STEVEN R (US)) 13 September 2001 (2001-09-13) cited in the application abstract	1-38
A	WO 00/66631 A (CAMBRIDGE ANTIBODY TECH ; TEMPEST PHILIP RONALD (GB); BRADDOCK PETA SA) 9 November 2000 (2000-11-09) the whole document	1-38
A	LING HONG ET AL: "Therapeutic role of TGF-beta-neutralizing antibody in mouse Cyclosporin A nephropathy: Morphologic improvement associated with functional preservation." JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY, vol. 14, no. 2, February 2003 (2003-02), pages 377-388, XP002289846 ISSN: 1046-6673 abstract	1-38
P,X	BENIGNI ARIELA ET AL: "Add-on anti-TGF-beta antibody to ACE inhibitor arrests progressive diabetic nephropathy in the rat." JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY, vol. 14, no. 7, July 2003 (2003-07), pages 1816-1824, XP002289847 ISSN: 1046-6673 the whole document	1-38

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/013677

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-38 (in part)
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1-38 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/013677

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0166140	A	13-09-2001	AU 7210001 A	17-09-2001
			CA 2400628 A1	13-09-2001
			EP 1263464 A1	11-12-2002
			JP 2004502644 T	29-01-2004
			WO 0166140 A1	13-09-2001
WO 0066631	A	09-11-2000	AU 768554 B2	18-12-2003
			AU 4588600 A	17-11-2000
			BR 0010162 A	05-02-2002
			CA 2370304 A1	09-11-2000
			EP 1175445 A1	30-01-2002
			WO 0066631 A1	09-11-2000
			GB 2350612 A , B	06-12-2000
			JP 2003501348 T	14-01-2003
			NO 20015261 A	21-12-2001
			NZ 514759 A	31-10-2003
			US 2003091566 A1	15-05-2003
			US 2003064069 A1	03-04-2003
			US 6492497 B1	10-12-2002